

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

REC'D 16 FEB 2005

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Applicant's or agent's file reference 4-32697A	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/1276	International filing date (day/month/year) 10.10.2003	Priority date (day/month/year) 11.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D239/90		
Applicant NOVARTIS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
 - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 23.04.2004	Date of completion of this report 15.02.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stix-Malaun, E Telephone No. +49 89 2399-8057 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/11276**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-23 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
 - ☐ the claims, Nos.:
 - ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
- (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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EXAMINATION REPORT**

International application No. **PCT/EP 03/11276**

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 12

because:

☒ the said international application, or the said claims Nos. 12 (Industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-13
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-11,13
	No: Claims	

2. Citations and explanations

see separate sheet

III NON-ESTABLISHMENT

Claim 12 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

- D1: WO 98/11438 A (TREGA BIOSCIENCES) 19 March 1998 (1998-03-19)
- D2: EL-SHARIEF, A.M.: "A COMPARATIVE STUDY OF THE BEHAVIOR OF CYANTHIOFORMAMIDE" HETEROATOM CHEMISTRY, vol. 13, no. 4, 2002, pages 291-8, XP008026391 US
- D3: FR-A-2 167 642 (PFIZER) 24 August 1973 (1973-08-24)
- D4: WO 01/70228 A (MERCK) 27 September 2001 (2001-09-27)
- D5: WO 98/18781 A (VERICOR) 7 May 1998 (1998-05-07)
- D6: WO 97/44041 A (MERCK) 27 November 1997 (1997-11-27)

have been considered for the examination procedure.

Due to a spelling mistake in the ISR of D3 it is not clear whether the applicant has retrieved the correct document. Therefore, a copy of D3 is sent to the applicant.

2. NOVELTY

The subject-matter of the claims is anticipated implicitly or explicitly by D3 (see p.2, intermediate of formula (V), p 4, formula (I), p 10, example IV, p.16, example 18, p. 17, example 33).

The subject matter of claim 5 is anticipated by D4 (see p. 34, step 1.1.A), D5 (see p. 35,), D6 (see p.13, fig 1, p.45, I.2, p.41, last line).

The claimed subject-matter of claims referring to formula (I) with or without the proviso is considered to be novel vis à vis D1 and D2: The essential structural dif-

ference between the claimed compounds and those of D1 resides at least in the presence of the substituent in position 3, it differs from D2 at least in the substitution in position 2 (Article 33(2) PCT).

3. INVENTIVE STEP

The compounds which are not novel lack inventive step as well.

However, for time-saving reasons inventive step is still assessed for novel compounds:

The subject-matter of the novel compounds according to formula (I) fulfils the requirements of Article 33(3) PCT for the following reasons:

The problem of the present application may be seen in the provision of further quinazolinone derivatives useful as anti-hyperalgesic agents.

The closest state of the art for the present application is represented by D1 and D3. D1 and D3 disclose structurally similar compounds having the same pharmaceutical properties which do not fall under the present application (see item novelty for D1). The products of D3 differ in the substitution at position 1.

None of the cited documents suggests a further substitution of the nitrogens. Accordingly the presently claimed solution does not seem to be obvious for the skilled person.

Under the assumption that the scope of the claims represents a reasonable generalisation of the tested examples, inventive step can be acknowledged for compounds according to formula (I).

It should be noted that in the regional phase it will become necessary to indicate at least one tested example in order to enable the skilled man to verify the scope of the claims.

The novel compounds of claim 5 are seen as simply analogous to those of D3-D6. Apart from this a special technical feature that combines independent claims is not detectable.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

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Thus, compounds according to formula (II) lack an inventive step.

4. INDUSTRIAL APPLICABILITY:

For the assessment of the present Claims 7-13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

INTERNATIONAL SEARCH REPORT

Internati plication No
PCT/EP 03/11276

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D239/90 C07D239/95 C07D405/04 C07C229/56 A61K31/517
A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 11438 A (TREGA BIOSCIENCES) 19 March 1998 (1998-03-19) page 1 -page 5; claims 1,2 ---	1,8-12
A	EL-SHARIEF, A.M.: "A COMPARATIVE STUDY OF THE BEHAVIOR OF CYANTHIOFORMAMIDE" HETEROATOM CHEMISTRY, vol. 13, no. 4, 2002, pages 291-8, XP008026391 US page 291 -page 294 X page 294 ---	1 5
A	FR 2 167 742 A (PFIZER) 24 August 1973 (1973-08-24) the whole document X page 1 -page 4 ---	1,8-12 5
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

14 January 2004

Date of mailing of the international search report

28/01/2004

Name and mailing address of the ISA

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Francois, J

INTERNATIONAL SEARCH REPORT

Internatl. Application No.
PCT/EP 03/11276

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 70228 A (MERCK) 27 September 2001 (2001-09-27) page 34; figure SHEM.A ----	5
X	WO 98 18781 A (VERSICOR) 7 May 1998 (1998-05-07) page 35 -page 37 ----	5
X	WO 97 44041 A (MERCK) 27 November 1997 (1997-11-27) page 41; figures SCHEME,A -----	5

INTERNATIONAL SEARCH REPORT

Inter application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 12 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internati

ication No

PCT/EP 03/11276

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9811438	A	19-03-1998	US 5783577 A AU 4416497 A WO 9811438 A1	21-07-1998 02-04-1998 19-03-1998
FR 2167742	A	24-08-1973	GB 1420309 A AU 471416 B2 AU 5079173 A BE 793737 A1 CA 983099 A1 DE 2300350 A1 DK 132298 B ES 410376 A1 FR 2167742 A1 IE 37058 B1 IT 974288 B LU 66799 A1 NL 7300139 A SE 400854 B	07-01-1976 29-04-1976 11-07-1974 05-07-1973 03-02-1976 12-07-1973 17-11-1975 16-12-1975 24-08-1973 27-04-1977 20-06-1974 19-04-1973 10-07-1973 10-04-1978
WO 0170228	A	27-09-2001	AU 4742101 A WO 0170228 A1	03-10-2001 27-09-2001
WO 9818781	A	07-05-1998	US 6025371 A US 6413724 B1 AU 6908398 A WO 9818781 A2	15-02-2000 02-07-2002 22-05-1998 07-05-1998
WO 9744041	A	27-11-1997	AU 712019 B2 AU 3141197 A CA 2254974 A1 EP 0920319 A1 JP 2000511186 T WO 9744041 A1 US 6150522 A	28-10-1999 09-12-1997 27-11-1997 09-06-1999 29-08-2000 27-11-1997 21-11-2000